Remarks

Amendments to the Specification:

Paragraph [0419] of the published application has been amended to delete the phrase "7-methylthio" from the chemical name reeited for Example 1. A person of ordinary skill in the art would recognize this amendment as a correction of an error since the starting material did not contain a methylthio group and none of the reagents used in reaction with the starting material contained a methylthio group. Therefore, the product cannot contain a methylthio group.

Paragraph [0430] has been amended to delete the reference to "Method 4" as it relates to the preparation of (R)-α-[N-(t-butoxycarbonylmethyl)carbamoyl]benzylamine. The deletion corrects a typographical error since (R)-α-[N-(t-butoxycarbonylmethyl)-carbamoyl]benzylamine does not appear in Method 4.

Applicants submit that no prohibited new matter has been introduced by either of these amendments.

Amendments to the Claims:

Claims 1, 4, 6, 7, 12, 13 and 18 have been amended. Elected claims 3, 5, 8 and 9 have been cancelled without prejudice or disclaimer of the subject matter encompassed therein, and with the understanding that Applicants may pursue these cancelled claims in a continuation application. Withdrawn claims 2, 10, 11 and 17 have been cancelled without prejudice or disclaimer of the subject matter encompassed therein, and with the understanding that Applicants may pursue these cancelled claims in a divisional application. Withdrawn process claim 13 has been amended to conform to the scope of composition claim 1. Accordingly, if product claim 1 is found allowable, Applicants submit that under MPEP 821.041, the withdrawn process claims (*e.g.*, claim 13) that depend from or otherwise require all the limitations of the allowable product claim should be rejoined.

The amendments to claims 1, 4, 6, 7, 12, 13 and 18 were made to conform the recited scope of these claims to the elected subject matter of Group 1 as identified by the Office Action (see the definition of Group I on page 4) and to replace the recited term "prodrug" with "*in vivo* hydrolysable ester or amide". Support for this replacement of the term "prodrug" may be found

in the specification of the corresponding published international application at, *inter alia*, page 11, lines 4 to 29. Applicants therefore submit that no prohibited new matter has been introduced by any of the amendments.

1. Rejection under 35 U.S.C. 112, second paragraph

Claims 1, 3 to 9, 12 and 18 are rejected as allegedly indefinite for use of the term "prodrug".

Claims 3, 5, 8 and 9 have been cancelled without prejudice or disclaimer of the subject matter encompassed therein, effectively mooting this rejection. Without acquiescing to the merits of the Examiner's rejection regarding remaining claims 1, 4, 6, 7, 12 and 18, Applicants have amended the these claims to replace the term "prodrug" with "*in vivo* hydrolysable ester or amide" which Applicants submit clearly defines the particular variations that may be made to selected atoms on the claimed compounds of the invention. As discussed above, this amendment is fully supported by the specification. Accordingly, Applicants respectfully request that this rejection be withdrawn.

2. Rejection under 35 U.S.C. 112, first paragraph

A. Scope of claims

Claims 1, 3 to 9 and 18 are rejected for allegedly lacking enabling disclosure in the specification. The Examiner does acknowledge the compounds of the invention of Group I as being enabled and presents an analysis using the *In re Wands* factors to support an assertion that the scope of the claims as filed is not enabled.

Claims 3, 5, 8 and 9 have been cancelled without prejudice or disclaimer of the subject matter encompassed therein, effectively mooting this rejection. Without acquiescing to the merits of the Examiner's rejection regarding remaining claims 1, 4, 6, 7 and 18, Applicants have amended these claims to conform to the scope of elected Group I as identified by the Examiner on page 4 of the current Office Action. Applicants therefore respectfully request that this rejection be withdrawn.

B. "Prodrug"

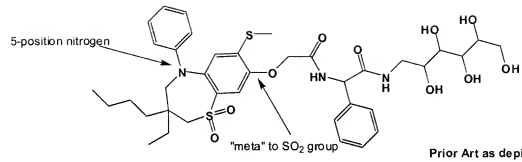
Claims 1, 3 to 9, 12 and 18 are rejected as allegedly lacking enabling disclosure in the specification for the recited claim term "prodrug". The Examiner presents an analysis under *In re Rainer, In re Colianni* and *Ex Parte Formal* to support an assertion that use of the term "prodrug" is not enabled.

As indicated above in rebutting the rejection of record under 35 U.S.C. 112, second paragraph, Applicants have cancelled claims 3, 5, 8 and 9 without prejudice or disclaimer of the subject matter encompassed therein, effectively mooting this rejection. Without acquiescing to the merits of the Examiner's rejection regarding remaining claims 1, 4, 6, 7, 12 and 18, Applicants have amended the these claims to replace the term "prodrug" with "*in vivo* hydrolysable ester or amide" which Applicants submit clearly defines the particular variations that may be made to selected atoms on the claimed compounds of the invention. As discussed above, this amendment is fully supported by the specification. Accordingly, Applicants respectfully request that this rejection be withdrawn.

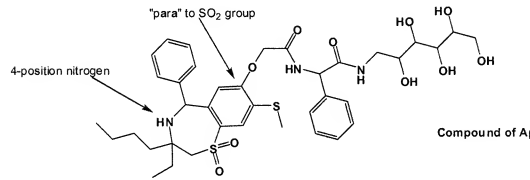
3. Rejection under 35 U.S.C. 103(a)

Claims 1, 3 to 9, 12 and 18 are rejected as allegedly obvious over WO 2003/020710 to Starke *et al.* ("Starke"). The Examiner indicates that the compounds described by Starke differ from the compounds claimed by Applicants only by the shift of a nitrogen atom from the 5-position of the benzothiazepine ring system (Starke) to the 4-position of the benzothiazepine ring system (Applicants). In view of this indication of structural similarity, the Examiner cites various court cases to support the finding of a *prima facie* case of obviousness where positional isomerism is observed. A diagram is provided by the Examiner that points out the asserted difference between the Starke compounds and Applicants' compounds.

Applicants submit that the claims as amended to conform to the elected invention of Group I, as defined by the Examiner, differ from the teaching of Starke in at least two respects. The following picture points out these differences:



Prior Art as depicted by Examiner



Compound of Applicants' claims

As acknowledged by the Examiner, the compounds of Applicants' claims contain a ring nitrogen at the 4-position of the benzothiazepine ring, while the compounds taught by Starke contain a ring nitrogen at the 5-position of the benzothiazepine ring. Further, Applicants submit that there is another significant structural difference between Applicants' claims and the prior art compound depicted by the Examiner. In Applicants' claims as amended, the Group IA substituent (*i.e.*, R^5) occupies a different position on the phenyl ring compared to the corresponding substituent in the prior art compound indicated by the Examiner. This additional difference does not appear in the Examiner's depiction of Applicants' compound because the Examiner has switched the relative positions of the R^5 and R^6 substituents on the phenyl ring. In formula (I) in Applicants' claim 1, the R^5 substituent is "para" to the sulfonyl group and the R^6 substituent is "meta" to the sulfonyl group.

Applicants submit that a person of ordinary skill in the art would not be motivated to make two structural changes to the Starke compounds to arrive at Applicants' compounds. Given the structural diversity of the compounds described in Starke, and the numerous possible sites available on the Starke compounds for manipulation, Applicants submit that it would be nonobvious and require undue experimentation for a person of ordinary skill to make the particular structural changes to the Starke compounds that are necessary to arrive at Applicants' claimed compounds. The court cases referenced by the Examiner to support his assertion of obviousness through positional isomerism, typically involve single changes to a specific compound. In the instant situation, there are two unrelated changes that are required to be made to a compound that itself is just one of thousands of compounds encompassed by the structural formulae described in Starke. Applicants submit that such an exercise – *i.e.*, selecting one compound from the thousands of compounds described in Starke, followed by altering the structure of that particular compound by making two unrelated changes – one change on the thiazepine ring and the other change on the benzene ring – would not be obvious to a person of ordinary skill in the art.

Applicants also note that it is surprising that making structural changes to known IBAT inhibitors, such as those described in Starke, result in compounds (such as those of the present invention) that maintain their effectiveness as IBAT inhibitors (see, *e.g.*, page 2, lines 20-21 of the corresponding PCT application).

For at least the above stated reasons, Applicants respectfully request that this rejection be withdrawn.

4. Obviousness-type Double Patenting

Claims 1, 3 to 9, 12 and 18 are rejected as allegedly unpatentable over claims 1 to 11 of U.S. Patent 7,192,946.

For at least the reasons provided in Section 3 of the response (see above), Applicants submit that Applicants' claims, as amended, are patentably distinct over the cited U.S. patent. Accordingly, Applicants respectfully request that this rejection be withdrawn.

5. Objections

The Examiner objects to the disclosure because of the assertion that Example 1 and Example 2 appear to be the same compound, based on the fact that they have identical names.

Applicants have amended the specification to remove the phrase "7-methylthio" from the name of the compound recited in Example 1. Applicants submit that such an amendment does not add prohibited new matter and simply constitutes correction of a typographical error. The starting material used in Example 1 does not contain a methylthio group and there is no reagent added to the starting material that contains a methylthio group. Therefore, a person of ordinary skill in the art would know that the resulting product cannot contain a methylthio group.

Regarding the reference in Method 6 to Method 4 as it relates to (R)-α-[N-(t-butoxycarbonylmethyl)carbamoyl]benzylamine, Applicants have deleted the reference to Method 4 as an error and submit that (R)-α-[N-(t-butoxycarbonylmethyl)carbamoyl]benzylamine was known as of the time of the filing of the subject application. See, *e.g.*, Method 86 on page 83 of European Patent 1345918 B1.

6. Conclusion

The foregoing amendments and remarks are being made to place the application in a better condition for allowance. Applicants respectfully request that the Examiner reissue a corrected restriction requirement. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which my be required, including any required extension of time fees, or to credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. 1.136(a)(3).

Respectfully submitted
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